REMARKS

This is in response to the Office Action mailed January 6, 2009, the time for a response to which has been extended to and through July 6, 2009.

Claims 1-7, 9, and 15-17 are pending in the application. Claim 17 has been canceled without prejudice. Claim 1 has been amended as discussed below.

REJECTION UNDER 35 USC 112, 1st PARAGRAPH, WRITTEN DESCRIPTION

At pages 2-7 of the Office Action, the Examiner rejected claims 1-7, 9, 15 and 16 under 35 USC 112, first paragraph as failing to comply with the written description requirement. It is not clear from the Office Action whether claim 17 was included in the rejection. In the present Office Action the Examiner alleged that there was insufficient written description of the invention because only a few heterocyclic rings are exemplified.

Applicants again traverse this rejection.

Claim 1 has been amended to delete the previously added definition of "heteroaryl," and insert the specific ring systems of claim 17. Claim 17 has been canceled without prejudice. Claim 1 has also been amended to delete the previously added definition of "heterocycloalkyl," and insert the specific heterocycloalkyl ring structures disclosed at page 13, lines 5-6 of the specification.

The Examiner alleged that a few examples have been given, but these are not commensurate with the scope of Applicants' claims.

Applicants again respectfully submit that the specification provides sufficient written description of the claimed compounds to satisfy the requirements of section 112, first paragraph. In order to satisfy the written description requirement of 112, first paragraph, the Applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the "written description" inquiry, whatever is claimed. *Vas Cath Inc. v. Mahurkur* 19 USPQ2d 1111, 1117 (Fed. Cir. 1991). Possession of the invention may shown in a variety of ways. One shows that

one is "in possession" of the invention by such descriptive means as words, structures, figures, diagrams, formulas, etc. that fully set forth the claimed invention. *Lockwood v. American Airlines* 41 USPQ2d 1961, 1966 (Fed. Cir. 1997). The Guidelines for Examination of Patent Applications Under the 35 USC 112, ¶ , "Written Description" Requirement, Federal Register, vol. 66, pages 1099-1111, 2001, referred to in this response as the "Written Description Guidelines," state that an Applicants may show possession of an invention by an actual reduction to practice, by disclosure of drawings or structural formulae that are sufficiently detailed to show that Applicant was in possession of the invention, or any description of distinguishing or identifying characteristics sufficient to show that Applicant was in possession of the claimed invention. (Written Description Guidelines, page 1104, right column).

In the present application, Applicants are claiming certain fredericamycin derivatives. The compounds have been described using chemical formulae and description of possible values for the variable substituents in the formulae. The formulae and variable substituents are defined and discussed in the specification. Claim 1 has been amended to state that "heteroaryl"and "cycloheteroaryl" mean the specific ring systems or groups recited in the claim. Persons skilled in the art are left in no doubt that Applicants were in possession of the claimed compounds when the application was filed, as they can obtain any particular embodiment by simply selecting a value for each for the variable substituents of the formulae of the claimed compounds.

Applicants have shown that they are in possession of the invention by means of the chemical formulae set out in the specification, and the examples of specific embodiments of the claimed compounds. The specification thus provides adequate written description of claims 1-7, 9, 15 and 16. Withdrawal of this section 112, first paragraph rejection is respectfully requested.

REJECTION UNDER 35 USC 112, 1st PARAGRAPH, ENABLEMENT

At pages 9-10 of the Office Action, the Examiner rejected claims 1-7, 9, 15 and 16 under 35 USC 112, first paragraph as not enabled for the reasons given in the previous Office Action. Again, it is not clear whether claim 17 was included in the rejection. In the present Office Action, the Examiner alleged that the pharmaceutical art coupled with the art of organic synthesis is highly unpredictable, and that Applicants have not provided guidance for the same.

The Examiner also alleged that the definitions for "heteroaryl" and "heterocycloalkyl" added to the claims in the previous amendment do not enable the claims.

Applicants again traverse this rejection. Claim 1 has been amended to delete the previously added definition of "heteroaryl," and insert the specific ring systems of claim 17. Claim 17 has been canceled without prejudice. Claim 1 has also been amended to delete the previously added definition of "heterocycloalkyl," and insert specific groups disclosed in the specification. The definitions of "heteroaryl" and "heterocycloalkyl" in claim 1 now refer to specific ring systems.

The test of enablement is whether one reasonably skilled in the art could make or use the invention from the disclosures in the patent coupled with information known in the art without undue experimentation. *United States v. Telectronics, Inc.*, 857 F.2d 778, 785, 8 USPQ2d 1217, 1223 (Fed. Cir. 1988). In the present Office Action, the Examiner alleged that the specification does not have enough examples of heteroaryl substituents to show that the full scope has been reduced to practice. Applicants disagree. There has never been a requirement that every species encompassed by a claim must be disclosed or exemplified in a working example. In re Angstadt, 537 F.2d 498 (CCPA 1976). In order to meet the enablement requirement, not all all embodiments of the claimed compounds need to be exemplified in the specification.

The definitions of "heteroaryl" and "heterocycloalkyl" in claim 1 have been amended to recite specific ring systems and groups. Persons skilled in the art can obtain any particular embodiment by simply selecting a value for each for the variable substituents of the formulae of the claimed compounds. Persons skilled in the art can thus make and use the compounds of amended claims 1-7 without undue experimentation.

According to the Examiner's comments in the previous Office Action, the claims are directed to methods of treatment that are not enabled because of lack of data or guidance showing that the claimed compounds actually treat tumors or parasites. Applicants continue to direct the Examiner's attention to MPEP 2107.03 "Special Considerations for Asserted Therapeutic or Pharmacological Utilities." Applicant does not have to prove that a correlation exists between a particular activity and an asserted therapeutic use as a matter of statistical certainty, nor does the applicant have to provide actual evidence of success in treating humans where such utility is asserted. Instead, all that is required is a reasonable correlation between the

activity and the asserted use. Courts have routinely found evidence of structural similarity to a compound known to have a particular therapeutic or pharmacological utility as being supportive of an assertion of therapeutic utility for a new compound. If reasonably correlated to the particular therapeutic or pharmacological utility, data generated using *in vitro* assays, or from testing in an animal model or a combination thereof almost invariably will be sufficient to establish therapeutic or pharmacological utility for a compound, composition or process. The specification at page 57, lines 1-4 in the section entitled "Biological activity against 12 cancer lines" and Table 7 presents data on the antitumor activity of the claimed compounds. The specification shows the averaged results of the efficacy of over twenty compounds of the invention in *in vitro* assays with twelve cancer cell lines, representing lung, breast, melanoma, renal, uterine, and prostate tumors. Adriamycin, cisplatin and fredericamycin, three known antitumor agents were also tested and the results shown in Table 7. In Table 7 the compounds of the invention are shown by a number in the left column that correlates with the example of the same number in the Example section beginning at page 58 of the specification. The claimed compounds showed efficacy in the assays comparable to fredericamycin, and often the IC70 was lower than the IC70 of fredericamycin.

As Applicants have previously argued, the compounds of claims 1-7 are derivatives of fredericamycin, a compound known in the art to have antitumor properties. The specification presents the same type of data as Yokoi et al., Misra and Kelly et al. to show antitumor properties of the compounds. Additionally, antitumor activity of the claimed compounds was compared with the activity of known antitumor agents, fredericamycin and adriamycin in the same assay. Fredericamycin derivatives in Yokoi et al. and Misra had both antitumor and antibacterial activity. Applicants continue to believe that they have shown a reasonable correlation between the activity of the compounds and the asserted uses.

For at least the reasons discussed above, the data presented in the specification is believed to be sufficient to enable to persons skilled in the art to make and use the claimed invention throughout its scope for treatment of the types of tumors recited in claim 15 and parasites. The specification thus enables claims 1-7, 9, 15 and 16. Withdrawal of this section 112, first paragraph rejection is again respectfully requested.

REJECTION UNDER 35 USC 103

At page 3 of the Office Action, the Examiner rejected claims 1-7, 9, 15 and 16 under 35 USC 103 as being *prima facie* obvious over U.S. patents 4,584,377 (Yokoi et al.); 4,673,678 (Misra) and 5,166,208 (Kelly et al.). Duan et al., Delgado et al. and Okimoto et al. were also used to reject the claims.

In the present Office Action, the Examiner stated that the claims still include sugars in the R substituents. The Examiner commented that claim 15 limits it to specific tumors, but it cannot be seen how this limitation can overcome the rejection. The Examiner also alleged that Duan et al., Delgado et al. and Okimoto et al. teach using cyclodextrin to make drugs more bioavailable, and provide motivation for adding poylethylene glycol or sugars to fredericamycin to make them more bioavailable and thus more effective.

Applicants traverse this rejection. Claim 1 has been amended to delete reference to sugars in substituents R5, R21 and R22.

A *prima facie* case of obviousness requires the following: (1) there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings; (2) there must be a reasonable expectation of success; and (3) the prior art reference (or references when combined) must teach or suggest all the claim limitations. MPEP at 2143.

The three cited patents, Yokoi et al., Misra and Kelly et al. each disclose fredericamycin A derivatives, but do not disclose or suggest the compounds of amended claims 1-7. Duan et al., Delgado et al. and Okimoto et al. teach using cyclodextrin to make drugs more bioavailable, but there is no disclosure of using cyclodextrin with fredericamycin.

The compounds of amended claims 1-7 do not contain sugars as a choice for any of the substituents. The combined teachings of the cited references do not disclose or suggest all of the limitations of the compounds of amended claims 1-7. The fredericamycin derivatives of claims 1-7, drugs of claim 9, and the methods of claims 15 and 16 are therefore not *prima facie* obvious in view of the combined teachings of Yokoi et al., Misra, and Kelly et al., Duan et al., Delgado et al. and Okimoto et al.

The compounds of claims 1-7, drugs of claims 9-10 and the methods of claims 15 and 16

are not *prima facie* obvious in view of the combined teachings of Yokoi et al., Misra, and Kelly et al. Duan et al., Delgado et al. and Okimoto et al. Withdrawal of this section 103 rejection is respectfully requested.

In view of the above, the present application is believed to be in a condition ready for allowance. Reconsideration of the application is respectfully requested and an early Notice of Allowance is earnestly solicited.

The Director is hereby authorized to charge any deficiency in the fees filed, asserted to be filed or which should have been filed herewith (or with any paper hereafter filed in this application by this firm) to our Deposit Account No. 03-2775, under Order No. 14528-00001-US.

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Respectfully submitted,

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